IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (GBW) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter Defendants.	[redacted] [redacted]

PLAINTIFF/COUNTER-DEFENDANTS' MEMORANDUM OF LAW IN SUPPORT OF ITS *DAUBERT* MOTION TO EXCLUDE TESTIMONY AND OPINIONS OF STEVEN F. DOWDY, PH.D.

Amanda S. Williamson (admitted *pro hac vice*)
Christopher J. Betti (admitted *pro hac* vice)
Krista V. Venegas (admitted *pro hac* vice)
Wan-Shon Lo (admitted *pro hac vice*)
Maria E. Doukas (admitted *pro hac vice*)
Zachary Miller (admitted *pro hac vice*)
Guylaine Haché (admitted *pro hac vice*)
Michael T. Sikora (admitted *pro hac vice*)
110 N. Wacker Drive, Suite 2800
Chicago, IL 60601
Telephone: 312.324.1000 | Fax: 312.324.1001
amanda.williamson@morganlewis.com
christopher.betti@morganlewis.com
krista.venegas@morganlewis.com
shon.lo@morganlewis.com
maria.doukas@morganlewis.com
zachary.miller@morganlewis.com
guylaine.hache@morganlewis.com
michael.sikora@morganlewis.com

Amy M. Dudash (DE Bar No. 5741)
MORGAN, LEWIS & BOCKIUS LLP
1201 N. Market Street, Suite 2201
Wilmington, DE 19801
Telephone: 302.574.3000 | Fax: 302.574.3001
amy.dudash@morganlewis.com

Alison P. Patitucci (admitted *pro hac vice*)
2222 Market Street
Philadelphia, PA 19103
Telephone: 215.693.5000 | Fax: 215.963.5001
alison.patitucci@morganlewis.com

Attorneys for Plaintiff/Counterclaim Defendant Nippon Shinyaku Co., Ltd. and Counterclaim Defendant NS Pharma, Inc.

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Plaintiff Nippon Shinyaku Co., Ltd. and NS Pharma, Inc. (collectively, "NS") hereby move this Court to exclude and strike certain portions of expert testimony by Defendants' expert Steven F. Dowdy, Ph.D.

I. NATURE AND STAGE OF THE PROCEEDING

NS incorporates by reference its statement regarding the nature and stage of the proceedings from its Motion for Partial Summary Judgment No. 1.

II. ARGUMENT

A. Dr. Dowdy Should be Precluded from Offering Opinions that Are Based on a New Construction for "Antisense Oligonucleotide."

Dr. Dowdy's opinions regarding written description and enablement apply a new claim construction for the term "antisense oligonucleotide" and should be excluded. "It is improper [for an expert] to argue claim construction to the jury because the 'risk of confusing the jury is high when experts opine on claim construction."' *CAO Lighting, Inc. v. Gen. Elec. Co.*, No. 20-681-GBW, 2023 WL 1930354, at *6 (D. Del. Jan. 30, 2023) (quoting *Cordis Corp. v. Boston Sci. Corp.*, 561 F.3d 1319, 1337 (Fed. Cir. 2009)).

Dr. Dowdy argues that a POSA would understand the term "antisense oligonucleotide" to mean that the entire oligonucleotide must be "highly complementary, if not 100% complementary" to the target region. Ex. 2 (Rebuttal Expert Report of Steven F. Dowdy, Ph.D. ("Dowdy Rebuttal") ¶ 37. Dr. Dowdy tries to excuse his belated re-interpretation of the claims by arguing that "the Court did not address whether the portion of the antisense oligonucleotide outside 'a base sequence,' if any, needs to be 100% complementary." *Id.* Dr. Dowdy is wrong. The parties already briefed whether the entire "antisense oligonucleotide" must be "complementary" during claim construction. *See, e.g.*, D.I. 166 at 24, 30-32, 41-43, 47-49

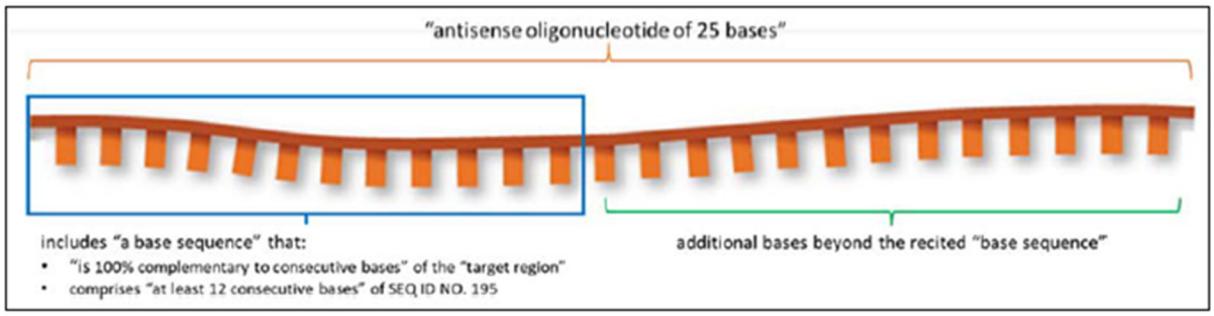
(briefing this issue in terms 1 and 1a). Counsel for Sarepta highlighted exactly that interpretive difference for the Court when presenting the parties' dispute over Terms 1 and 1a at the hearing:

> Sarepta's construction requires that **the antisense oligonucleotide be 100 percent complementary** to its target. **Nippon Shinyaku's alternative construction does not require 100 percent complementarity** for the antisense oligonucleotide, but only for a portion of it. **So only part of the oligonucleotide needs to be complimentary.**

Ex. 17 (Claim Constr. Hr'g Tr.) at 6:13-25; *see also* D.I. 171 (Ex. 37), Stein Op. Decl. ¶ 68 ("A skilled artisan would have understood that all of the bases of the claimed antisense oligonucleotide form a base sequence and are complementary to the target region, not just 'any' 'part' of the bases as NS's strained construction implies.").

The Court resolved this dispute in NS's favor. It determined that the "100% complementary" limitation did not apply to the entire "antisense oligonucleotide." D.I. 248 at 9-10. The Court explained that "Sarepta improperly conflates the claims' requirement for 'a base sequence'—that it be '100% complementary to consecutive bases in a target region'—to the entire 'antisense oligonucleotide.'" *Id.* at 10.

As discussed at length during the *Markman* briefing (D.I. 166) and hearing (Ex. 17), and as shown in the figure below, the "**base sequence**" of the claims, outlined in **blue**, includes at least 12 bases of SEQ ID NO. 195 and must be **100% complementary** to the target region of exon 53 pre-mRNA. D.I. 166 at 20. For an exemplary 25-base AO, the remaining 13 bases are unrecited and need not be complementary, consistent with the Court's construction. D.I. 248 at 9 (Court explaining that "the claimed antisense oligonucleotide includes at least 'a base sequence,' while allowing for additional elements, e.g., additional bases.").



D.I. 166 at 21. Yet, Dr. Dowdy seeks to improperly extend the "blue" box to all or nearly all of the unrecited bases, contrary to the Court's construction.[1]

Dr. Dowdy's analysis on written description and enablement is infected by this improper construction and should be struck. *See, e.g.*, Ex. 2 (Dowdy Rebuttal) at 9-166. Claim scope—and particularly the size of the claimed genus—are core considerations in written description and enablement challenges. And indeed, Dr. Dowdy prominently points to his new "antisense oligonucleotide" construction as the source of his disagreement with NS's experts on these foundational issues. *See, e.g.*, *id.* ¶¶ 35-41 (disputing scope of claimed genus based on new "antisense" construction); Ex. 13 (Dowdy Dep.) at 15:14-24 ([redacted]). By analyzing the claims under his (far narrower) construction, Dr. Dowdy has not offered opinions on written description and enablement of the claimed genus under the Court's construction and they therefore must be excluded.[2]

[1] To the extent Sarepta argues that Dr. Dowdy's new construction should be permitted because he is construing a different term, i.e., "antisense" vs. "a base sequence," that argument fails. *TwinStrand Biosciences, Inc. v. Guardant Health, Inc.*, No. 21-01126-GBW, D.I. 507 at 8 n.4 (D. Del. Oct. 31, 2023) ("It is immaterial that Dr. Quackenbush is construing a different term. The Court rejected this requirement and re-raising it in a different term is improper.").

[2] At the very least, the Court should strike Dr. Dowdy's genus calculations found in paragraphs 57-58 and Exhibit C of his Rebuttal Report (Ex. 2), which depend on his improper new construction.

B. Dr. Dowdy Should be Precluded from Offering Improper Opinions on Matters Related to Inequitable Conduct.

Sarepta contends that the NS Patents are unenforceable due to inequitable conduct because NS purportedly "misled" the Patent Office and "withheld" certain data and prior art during the prosecution of those patents. To succeed, Sarepta "must prove by clear and convincing evidence that the applicant knew of [a nondisclosed] reference, knew that it was material, and made a deliberate decision to withhold it." *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1290 (Fed. Cir. 2011). "[A]s a general matter, the materiality required to establish inequitable conduct is but-for materiality." *Id.* at 1290. "Determining but-for materiality requires that the court place itself in the shoes of a patent examiner and determine whether, had the reference(s) been before the examiner at the time, the claims of the patent would have still issued." *Regeneron Pharms., Inc. v. Merus N.V.*, 864 F.3d 1343, 1351 (Fed. Cir. 2017).

Sarepta relies on Dr. Dowdy's opinions to support its allegations that NS "misled" and "withheld" material information from the Patent Office. Specifically, Dr. Dowdy opines that NS "[redacted]." Ex. 1 (Opening Expert Report of Steven F. Dowdy, Ph.D. ("Dowdy Opening") ¶ 751. According to Dr. Dowdy, "this withheld information, and the misrepresentations made during prosecution, were material to the patentability of the NS Patents." *Id.* Dr. Dowdy further opines that "NS engaged in a pattern of withholding material information during the filing and worldwide prosecution of the NS Patents, and in opposing other patents directed to exon 53 targeting ASOs." *Id.*

The Court should exclude Dr. Dowdy's opinions on "materiality" as unreliable because he does not have the requisite experience with Patent Office practices to opine on such matters. To the extent courts allow expert conclusions on materiality, they must come from a person

"who has knowledge of and experience with the procedures of the PTO." *Lecat's Ventriloscope v. MT Tool & Mfg.*, 351 F. Supp. 3d 1100, 1115 (N.D. Ill. 2018) (citation and internal quotes omitted); *see also J&M Indus., Inc. v. Raven Indus., Inc.*, 457 F. Supp. 3d 1022, 1047 (D. Kan. 2020) (excluding technical expert's materiality opinion because "[t]hese are not opinions within her expertise"). Here, Dr. Dowdy lacks specialized training or experience with Patent Office examination procedures. He is not a member of the patent bar (Ex. 13 (Dowdy Dep.) at 126:9-10), he is not qualified to practice before the Patent Office (*id.* at 126:11-13), and he admitted that he has no practical experience with patent examination (outside of being a named inventor on a handful of patents) (*id.* at 126:14-25). Materiality is assessed from the perspective of a patent examiner, and Dr. Dowdy conceded that [redacted] *Id.* at 135:9-16. Because Dr. Dowdy lacks specialized training, knowledge, or experience regarding patent examination and procedure, Dr. Dowdy is not qualified to make "materiality" determinations from an inequitable conduct perspective.[3] His use of legal terminology characterizing information as "material information" or as "material to patentability" will no doubt confuse the jury and prejudice NS.[4]

The Court should also preclude Dr. Dowdy from offering opinions regarding the intent or state of mind of the NS inventors and NS's prosecution counsel. An expert may not "plumb the inventor's and attorneys' minds and discern whether they lacked candor or had actual intent to

[3] Sarepta's expert on patent examination and procedure, Mr. Hirshfeld, [redacted] Ex. 14 (Hirshfeld Dep.) at 69:5-70:9.

[4] To be clear, NS is not seeking to preclude Dr. Dowdy from offering opinions about technical aspects of the claimed invention, the prior art, and data NS allegedly "withheld" from the Patent Office, and how, in his opinion, this affects the validity of the NS Patents. But Dr. Dowdy's opinions did not end here. Dr. Dowdy repeatedly opines throughout his reports that the withheld information was "material to patentability." It is these opinions that NS seeks to preclude.

deceive during [the patent prosecution process]" because an expert's "education, training, and experience" does not qualify him to read minds. *Bone Care Int'l LLC v. Pentech Pharms., Inc.*, No. 08-1083, 2010 WL 3928598, at *9 (N.D. Ill. Oct. 1, 2010) (citation and internal quotes omitted); *see also Zimmer Surgical, Inc. v. Stryker Corp.*, 365 F. Supp. 3d 466, 498 (D. Del. 2019) (precluding an expert from testifying as to "an explicit credibility determination regarding [plaintiff's] prior patent counsel's statements to the PTO").

Dr. Dowdy's expert reports are replete with speculative accusations that the NS inventors and NS's prosecution counsel "withheld," "misrepresented," and made "misleading" statements to the Patent Office during prosecution of the NS Patents. Ex. 1 (Dowdy Opening) at p. 299, Heading XI (**misled**); *id.* at p. 300, Heading A (**misleading**); *id.* at p. 308, Heading 2 (**withheld** and **misrepresented**); *id.* ¶¶ 650, 651, 655, 661, 662, 666, 667, 669, 676, 679, 703, 704, 707, 709 (**withheld**); *id.* ¶ 678 (**misrepresentations**); *id.* ¶ 735 (**pattern of withholding**); *id.* ¶ 751 (**withheld**, **misrepresentations** and **pattern of withholding**). Implicit and necessary to such accusations are unfounded assertions that these individuals were aware of this allegedly "withheld" information (rather than simply not recalled, overlooked, or deemed not relevant), that they intended to present information in a way that was an alleged "misrepresentation" (rather than a subjective conclusion open to multiple interpretations), and that they intended to "mislead" the Patent Office (rather than make a good-faith argument favoring patentability).

Moreover, Dr. Dowdy states that "[redacted]" Ex. 1 (Dowdy Opening) ¶ 666. However, the deposition testimony relied on by Dr.

Dowdy does not support these assertions. *Id.* Dr. Dowdy points to the following deposition testimony as support:

[redacted]

The cited testimony does not show that [redacted] was aware of any of the representations made to the Patent Office during prosecution of the NS Patents. Indeed, Sarepta's

[5] Sarepta has offered no evidence that [redacted] was at all involved in the prosecution of the NS Patents. And [redacted] testimony confirms that he did not communicate with any of the US patent attorneys involved in prosecuting the NS Patents. Ex. 20 ([redacted] at 213:15–18 ([redacted]; *id.* at 213:19–25 ([redacted]); *id.* at 214:10–19 ([redacted]).

counsel did not even question [redacted] about those representations. Moreover, Dr. Dowdy did not consider the deposition transcript of Zhengyu Feng, Ph.D., who prosecuted the NS Patents, when forming his opinions. Ex. 1 (Dowdy Opening Appendix B, Materials Considered) at 11. That Dr. Dowdy purports to offer opinions as to the state of mind and intent of "prosecution counsel" (*id.* ¶ 751) without even considering the testimony of Dr. Feng demonstrates the unreliability of his assertions. Thus, any opinion from Dr. Dowdy about the intent or state of mind of the inventors or prosecution counsel, including that they "withheld," "misrepresented," "misled" or engaged in a "pattern" of "withholding" "material information" from the Patent Office, would be speculative, unreliable, and improper. *Bone Care*, 2010 WL 3928598, at *9; *Zimmer*, 365 F. Supp. 3d at 498.

Thus, NS respectfully requests that Dr. Dowdy be precluded from testifying that NS purportedly "misled" the Patent Office and "withheld" certain data and prior art during the prosecution, and that these alleged "misrepresentations" and this allegedly "withheld" information were "material to patentability" expressed on page 299 (Heading XI), page 300 (Heading A), page 308 (Heading 2), page 321 (Heading d), page 322 (Heading B and 1), page 334 (Heading 2), page 336 (Heading 3), page 343 (Heading 4), page 344 (Heading 5), page 349 (Heading C), and in paragraphs 1, 634, 635, 649, 650, 651, 655, 656, 661, 662, 666, 667, 669, 676, 678, 679, 684, 686, 690, 700, 701, 703, 704, 707, 709, 724, 732, 734, 735, 744, 748 and 751 of his Opening Report (Ex. 1), and on page 64 (Heading VI), and in paragraphs 1, 121, 124, 144, 145, 146, 151, 152, 156, 157, 158, 159, 167 n.29, 180, 194, and 246 of his Reply Report (Ex. 3).

C. Dr. Dowdy Should be Precluded from Relying on the Improperly Filed IPRs to Support His Opinions on Obviousness.

Dr. Dowdy opines that the Patent Trials and Appeals Board ("PTAB")'s preliminary decisions in the improperly filed *inter partes* reviews ("IPRs") "reinforce my opinion that the

asserted claims of the NS Patents would have been obvious as of August 2011." Ex. 1 (Dowdy Opening) ¶ 619. Dr. Dowdy should be precluded from relying on these PTAB decisions at trial. First, the Federal Circuit found that Sarepta filed these IPRs in breach of the parties' Mutual Confidentiality Agreement. *Nippon Shinyaku Co. v. Sarepta Therapeutics, Inc.*, 25 F.4th 998, 1006 (Fed. Cir. 2022). Sarepta should not benefit from its improperly filed IPRs at trial.

Second, the conduct and outcome of the IPRs are not relevant and would be confusing, misleading, prejudicial, and a waste of time. Courts in this District and elsewhere routinely exclude reference to factual findings, decisions, and legal conclusions from IPRs and other PTAB proceedings as having minimal probative value that is substantially outweighed by the potential for prejudice and confusion. *See, e.g.*, *IOENGINE, LLC v. PayPal Holdings, Inc.*, Nos. 18-452 & 18-826, 2022 WL 2800911, at *1 (D. Del. June 27, 2022) (Judge Bryson) ("PTAB's findings would be likely to confuse the jury and risk that the jury would decide the issues on evidence not before it."); *Integra LifeSciences Corp. v. HyperBranch Med. Tech., Inc.*, No. 15-819, 2018 WL 2186677, at *1 (D. Del. May 11, 2018) (Stark, J.) ("[T]he prejudice and confusion inherent in presenting [evidence regarding PTAB proceedings] to the jury—particularly given the PTAB's different standards—substantially outweighs its probative value."); *see also Vaporstream, Inc. v. Snap Inc.*, No. 17-00220, 2020 WL 978731, at *8 (C.D. Cal. Feb. 28, 2020).

Thus, the Court should preclude Dr. Dowdy from offering any testimony regarding Sarepta's improperly filed IPRs as expressed at page 307 (footnote 27) and page 352 (footnote 32), and in paragraphs 618-621 of his Opening Report (Ex. 1), and at page 48 (footnote 23) of his Reply Report (Ex. 3).

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Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

/s/Amy M. Dudash

Amy M. Dudash (DE Bar No. 5741)
1201 N. Market Street, Suite 2201
Wilmington, Delaware 19801
Telephone: 302.574.3000
Fax: 302.574.3001
amy.dudash@morganlewis.com

Attorneys for Plaintiff/Counterclaim Defendant Nippon Shinyaku Co., Ltd. and Counterclaim Defendant NS Pharma, Inc.

Amanda S. Williamson (admitted *pro hac vice*)
Christopher J. Betti (admitted *pro hac* vice)
Krista V. Venegas (admitted *pro hac* vice)
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Guylaine Haché (admitted *pro hac vice*)
Michael T. Sikora (admitted *pro hac vice*)
110 N. Wacker Drive, Suite 2800
Chicago, IL 60601
Telephone: 312.324.1000
Fax: 312.324.1001
amanda.williamson@morganlewis.com
christopher.betti@morganlewis.com
krista.venegas@morganlewis.com
shon.lo@morganlewis.com
maria.doukas@morganlewis.com
zachary.miller@morganlewis.com
guylaine.hache@morganlewis.com
michael.sikora@morganlewis.com

Alison P. Patitucci (admitted *pro hac vice*)
2222 Market Street
Philadelphia, PA 19103
Telephone: 215.693.5000
Fax: 215.963.5001
salison.patitucci@morganlewis.com